This symposium also marks a threshold in the research on the endoplasmic reticulum and ribosomes. Roberts noted further in his introduction that the case for protein synthesis by the ribosomes was still inconclusive. Several of the reasons he listed had to do with technical problems in demonstrating the connection, but one focused on the absence of a conception of the responsible mechanism: "No mechanism has been suggested which shows how the structure of the particle is compatible with its function as the template for synthesis of long chains" (p. vii). The mechanism that Palade had described treated the ribosome as a unit with an operation which interacted with the operations of the endoplasmic reticulum. It had not explained the operation of the ribosome itself.

Discovering the mechanism by which the ribosome synthesized proteins required moving to a yet lower level of organization at which research could focus on the chemical structures that comprised the ribosome or interacted with it. As was the case with the mitochondrion, research at this level was chiefly the province of biochemists and practitioners of two other new disciplines, biophysics and molecular biology, not researchers affiliating with cell biology. Since the research contributing to a basic sketch of the mechanism of protein synthesis in the ribosome is illustrative of one strategy for developing an account of a mechanism, I will briefly analyze it before returning to research in cell biology focusing on the transport of the newly created proteins.[33]

Going to a Lower Level: Decomposing the RNA Machinery

The biochemical research so far focused only on the process of making peptide bonds, but synthesizing proteins required linking amino acids in appropriate orders. Zamecnik (1958) proposed that protein synthesis involved "some biological equivalent of a printing press" that would specify the order and that the "press or template . . . is very likely RNA" (p. 120). He then advanced a scheme, initially proposed by Victor Konigsberger and Theo Overbeek, according to which amino acids are first activated by binding with an enzyme and a molecule of ATP, resulting in the transfer of the phosphate bond to an amino acid. He proposed that the amino acids bonded sequentially on the RNA template, and by what he characterized as a "zipper reaction" bonds were established between adjacent amino acids. In the final step in his

[33] For a discussion of the discovery of the mechanism of protein synthesis that emphasizes the interaction of molecular biology with biochemistry, see Darden and Craver (2002).

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